

**Amendment to the Specification:**

Please amend the specification in accordance with the following:

Delete the paragraph on page 1, beginning on line 4, and replace it with the following paragraph:

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This application is a continuation of co-pending U.S. patent application number 09/801,676, filed March 9, 2001. U.S. patent application number 09/801,676 was filed as a continuation of U.S. patent application number 09/459,996, filed December 14, 1999 (U.S. Patent 6,214,293). U.S. patent application number 09/459,996 was filed as a continuation of 08/853,459, filed May 9, 1997 (U.S. Patent 69,036,920), which claimed priority to U.S. provisional application number 60/017,860, filed May 9, 1996, all of which are incorporated herein by reference in their entireties.

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Amend the paragraph on page 17 beginning on line 7, as follows:

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Figures 8A and 8B show shows the results of a miniaturized microplate thermal shift assay of aprosulate binding to the D(II) domain of human FGF receptor 1.

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Amend the first paragraph on page 5 as shown below:

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Like calorimetric technologies, spectral technologies have been used to monitor temperature induced protein unfolding (Bouvier, M. *et al.*, *Science* 265:398-402 (1994); Chavan, A.J. *et al.*, *Biochemistry* 33:7193-7202 (1994); Morton, A. *et al.*, *Biochemistry* 1995:8564-8575 (1995)). ~~The calorimetric and spectral thermal shift studies described above all share a common limitation. In each study, only one binding reaction was heated and assayed at a time.~~ The single sample heating and assay configuration, as conventionally performed, has impeded the application of thermal shift technologies to high throughput screening of combinatorial libraries. Thus, there is a need for a thermal shift technology which can be used to screen combinatorial libraries, can be used to identify an drank lead compounds, and is applicable to all receptor proteins.

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Amend the paragraph starting on page 70, line 4, and ending on page 70, line 15, as shown below:

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Using the computer controlled process DirectedDiversity® (*see* U.S. Patent Number 5,463,564), scientists at 3-Dimensional Pharmaceuticals, Inc. have generated a combinatorial library of compounds directed at the active site of human  $\alpha$ -thrombin. Approximately 400 compounds were synthesized and assayed by a conventional spectrophotometric kinetic assay in which succinyl – Ala-Ala-Pro-Arg-p-nitroanilide (SEQ ID NO:1) (Bachem, King of Prussia, PA) served as the substrate. Five of these compounds, which are characterized by  $K_i$ 's that span almost four orders of magnitude in binding affinity, were used to test the range and limits of detection of the thermal shift assay. These five proprietary compounds are listed in Table 3, along with the  $K_i$  for each respective compound, as measured by the kinetic assay (last column).  $K_i$ 's for these compounds ranged from 7.7 nM for 3dp-4026 to 20.0  $\mu$ M for 3dp-3811.

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Amend the current version of the paragraph starting on page 19, line 1, and ending on page 19, line 2, to read:

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**Figure 27** is a schematic diagram of a method of screening biochemical conditions that optimize protein folding. This method employs denatured protein tagged with H-H-H-H-H-H (SEQ ID NO: 2) or R-R-R-R-R-R (SEQ ID NO: 3).

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Please insert the sequence listing at the end of the application.

**Amendments to the Drawings:**

Please make the following amendments to the drawings:

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Replace FIG. 8 with FIGS. 8A and 8B, as shown in the drawings submitted with the concurrently filed Request to Approve Proposed Drawing Corrections.

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Amend FIGS. 25 and 41A as shown in red in the drawings submitted with the concurrently filed Request to Approve Proposed Drawing Corrections.

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